89. The method of Claim 44, wherein the DNA transcription unit is administered parenterally to a mammal.

REMARKS

Claims 1-3, 5-7, 9-26, 28-38, 40-43, 52-61, 65-66, 73 and 75-77 have been canceled. Claims 81-89 have been added. Support for these claims is found throughout the Specification and particularly in canceled Claims 2, 3, 13, 14, 15, 17-23 and 32. No new matter has been added.

Claims 44-51, 62-64, 67-72, 74 and 78-80 are pending.

For the Examiner's convenience, the remainder of this Amendment is set forth under appropriate headings, in the order in which the issues were raised in the Office Action.

Table 6

The Examiner stated that Table 6 appeared to contain an error, in that there were two rows in the Table with data for intranasal (in) administration, while the same data in Table 7 of U.S. patent 5,643,578 indicates that the data showing 10/12 survival was for intravenous (iv) administration. Table 6 has been corrected to indicate that intravenous (iv) administration yielded 10/12 survival, whereas intranasal (in) administration yielded 13/17 survival. Support for this amendment is found particularly at page 25 lines 15-23, where it is indicated that excellent survival occurred in groups receiving intramuscular (im) inoculations, intravenous (iv) inoculations, or inoculations by each of three routes; and that good survival, but more severe influenza, occurred in those receiving intranasal inoculation.

Rejection of Claims under 35 U.S.C. §101

The Examiner rejected Claims 6, 7, 25, 26 and 52 as claiming the same invention as that of Claims 14-18 of U.S. Patent 5,643,578. Claims 6, 7, 25, 26 and 52 have been canceled.

Rejection of Claims under the Judicially Created Doctrine of Obviousness-type Double Patenting

The Examiner rejected Claims 1-3, 5, 9-24, 28-38, 40-51, 53-61 and 75-77 as being unpatentable over Claims 1-13 of U.S. patent 5,643,578. Claims 1-3, 5, 9-24, 28-38, 40-43, 53-61 and 75-77 have been canceled; therefore, only Claims 44-51 are at issue.

The claims of U.S. Patent 5,643,578 are to methods of immunizing a vertebrate against an infectious agent, by administering to the vertebrate a DNA transcription unit comprising DNA encoding a hemagglutinin of the infectious agent operatively linked to a promoter region, and methods of immunizing a vertebrate against influenza virus, by administering to the vertebrate a DNA transcription unit comprising DNA encoding an influenza virus antigen operatively linked to a promoter region.

Claims 44-51 do not encompass overlapping subject matter with the claimed invention of U.S. Patent 5,643,577, because the virus, as well as the antigen, differs from that in U.S. Patent 5,643,577. Claims 44-51 are drawn to methods of immunizing a mammal against an *immunodeficiency virus*, by administering to the mammal a DNA transcription unit comprising DNA encoding an antigen of the immunodeficiency virus operatively linked to DNA which is a promoter region. Immunodeficiency viruses do not have hemagglutinin.

Therefore, this rejection is obviated.

Rejection of Claims under 35 U.S.C. §112, second paragraph

The Examiner rejected Claims 2, 5-9, 10, 12, 18 and 34 as being indefinite, in that Claim 5 (and therefore Claims 6-10 which depend, directly or indirectly, from Claim 5) depended from canceled Claim 4; that Claim 12 recited "the mammal" without antecedent basis; and that Claims 2, 18 and 34 were unclear in the use of the term "nonretroviral".

Claims 5 and 12 have been canceled. Claims 2, 18 and 34 have also been canceled; however, Claim 81, which parallels canceled Claims 2, 18, and 34, includes the language suggested by the Examiner, stating that the promoter is not of retroviral origin. Support for this language is found throughout the Specification, and particularly, for example at page 20, Example 3, lines 21 *et seq*.

Rejection of Claims under 35 U.S.C. 112, first paragraph

The Examiner rejected Claims 1-3, 5, 6, 11-25, 30-37, 42, 43, 52-58, 61 and 75, stating that the specification was enabling for the invention wherein the antigen is an influenza virus hemagglutinin, but did not provide enablement for the invention when the DNA transcription unit encoded any other type of protein. In particular, the Examiner stated that Applicants have not provided convincing evidence that treatment with DNA vectors encoding antigens of SIV and HIV elicits protective immunity and that Dr. Robinson's first declaration showed that the method failed to protect the treated animals from SIV infection and death by AIDS.

Applicants' Attorney respectfully disagrees with this assessment of Dr. Robinson's first declaration. As described in the Specification at page 7, lines 5-11, "immunizing" refers to production of an immune response which protects, *partially or totally*, from the manifestations of infection (i.e., *disease*) caused by the infectious agent. Dr. Robinson's first declaration demonstrates successful immunization of macaques: four monkeys in the multiple route group were protected against manifestations of disease throughout the trial, and were free of clinical signs of AIDS at the time they were killed. Furthermore, partial protection from the manifestations of infection was demonstrated by reduction of viral loads to chronic levels more rapidly in the immunized animals than in the control animals. Therefore, Applicants have demonstrated successful immunization against SIV, which protected against disease during the course of the trial.

Objection to the Specification under 35 U.S.C. 112, first paragraph

The Examiner objected to the Specification, stating that the specification did not enable a person skilled in the art to make and use the invention. In particular, the Examiner stated that it is impossible to determine whether observation of a given immune response to an immunodeficiency virus vaccine in an animal model indicates that the tested vaccine actually confers protection against the virus. However, as discussed above, Applicants have actually demonstrated protection against disease caused by SIV in macaques; this protection against disease was demonstrated not in an animal model, but in animals which

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are the natural hosts for the virus.

With regard to HIV, the Examiner stated that one skilled in the art would not have regarded Applicants' results with the anti-SIV vaccine as being correlative with outcome or efficacy of a similar vaccine in a human. In making this determination, the Examiner cited Weiss (Washington Post, page A2, 4/30/97). The Weiss reference was published after Applicants' filing date and, therefore, should not be considered as being relevant to the state of the art at the time the application was filed.

The Specification describes in detail (see Example 12, page 49 *et seq.*) immunogenicity tests of HIV-based constructs. The HIV constructs generated neutralization activity in the immunized mice, as well as cytotoxic T cell activity. One of ordinary skill in the art, given these teachings regarding the immunogenicity of the HIV constructs, as well as the teachings of the Specification regarding protection against disease caused by SIV, would have reasonably concluded that the HIV constructs would behave similarly to the SIV constructs, and thereby confer protection against disease.

Rejection of Claims under 35 U.S.C. 112, first paragraph

The Examiner rejected Claims 9, 10, 28, 29, 40, 41, 44-51 and 62-74 for the reasons set forth in the objection to the Specification. In view of the discussion presented above, this rejection is obviated.

Rejection of Claims under 35 U.S.C. 102(b)

The Examiner rejected Claims 57, 59, 75, 76, and 77 as being anticipated by Townsend *et al.* These Claims have been

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canceled, thereby obviating this rejection.

The Examiner rejected Claims 62 and 65 as being anticipated by Cheng *et al.*, who disclose vectors containing DNA encoding SIV Rev and Env. As amended, Claims 62 and 65 pertain to transcription units containing specific HIV constructs (pCMV/HIV-1-NL4-3.dpol, pCMV/HIV-1-HXB-2.env, pCMV/HIV-NL4-3.env, JW4303/HIV-1-HXB-2.sgp120, and JW4303/HIV-1-HXB-2.sgp140) that are described in the Specification. Cheng *et al.* do not describe such HIV constructs; therefore, the claimed invention is not anticipated by Cheng *et al.*

The Examiner rejected Claims 62, 66, 68, 73, 78 and 79 as being anticipated by Rekosh *et al.*, who describe expression vectors containing a promoter operably linked to DNA encoding Env and tat gene products of HIV. Rekosh *et al.* do not describe the specific HIV constructs that are recited in the amended Claims; therefore, the claimed invention is not anticipated by Rekosh *et al.*

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CONCLUSION

In view of the discussion presented above, the claims, as amended, are in condition for allowance. Therefore, Applicant's Attorney respectfully requests that the Examiner reconsider and withdraw all rejections.

If the Examiner feels that a telephone conversation would expedite prosecution, the Examiner is invited to call the undersigned Attorney at (915) 845-3558. If the undersigned Attorney cannot be reached, the Examiner is invited to call Patricia Granahan at (781) 861-6240.

Respectfully submitted,

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